SITC 2022 LBA Abstract: TACTI-002 Part A

Combining the antigen-presenting cell activator eftilagimod alpha (soluble LAG-3) and pembrolizumab: efficacy results from the 1st line non-small cell lung cancer cohort of TACTI-002 (Phase II)

Short title: Phase II study of an APC activator combined with an anti-PD-1 antibody in 1st line metastatic NSCLC

Background: Eftilagimod alpha (E) is a soluble LAG-3 protein binding to a subset of MHC class II molecules to mediate antigen-presenting cell (APC) activation & T-cell (CD4/CD8) recruitment/activation. By stimulating APCs with E, T cells are recruited, possibly leading to stronger anti-tumor responses than with pembrolizumab (P) alone, especially in tumors not overexpressing PD-L1. Herein we report results of the 1st line non-small cell lung carcinoma (NSCLC) cohort in the TACTI-002 ("Two ACTive Immunotherapies") trial.

Methods: Pts with measurable, 1st line metastatic NSCLC unselected for PD-L1 were recruited. The objective response rate (ORR) by iRECIST was the primary endpoint (EP). Secondary EPs include ORR by RECIST 1.1, ORR by blinded independent central read (BICR), duration of response (DoR), progression-free survival (PFS), overall survival (OS), PD-L1 and IFN-gamma, safety & tolerability. Pts received 30mg E SC q2w for 8 cycles (1 cycle= 3 weeks) & then q3w for up to 1 year with P (200 mg IV q3w for up to 2 years). Imaging was done every 8 weeks & assessed by investigator. PD-L1 was assessed centrally (22C3 antibody). The study was powered to detect a 52% increase in ORR compared to historical results for P 80% power & 1-sided alpha of 2.5%. Planned recruitment=110 pts.

Results:
From Mar 2019-Nov 2021, 114 pts were enrolled. Median follow-up was 13 mo (data cut-off Jul 1st 2022). Median age was 67 yrs (44-85) & 74% were male. ECOG PS was 0 & 1 in 37% & 63% of pts. Pts presented with squamous (35%) or non-squamous (63%) carcinoma and 93% had metastatic disease. All PD-L1 subgroups were represented (Table 1). Pts received median 9.0 (range 1–18) P & 13.0 (1-22) E. 11 (9.6%) pts discontinued due to related adverse events (AEs). Common (≥15%) AEs were dyspnea (35%), asthenia (33%), decreased appetite (25%), cough (25%), anemia (23%), fatigue (21%), pruritus (21%), constipation (18%), nausea (17%), hemoptysis (16%) & diarrhea (16%).
ORR by iRECIST (primary EP) was 39.5% (95% CI 30.5-49.1) & median PFS was 6.9 mo (95% CI 4.9-9.3). Responses were observed in all PD-L1 subgroups (Table 1). ORR (iRECIST) for squamous & non-squamous were 37.5% & 38.9%. Median duration of response was 21.6 mo. Results acc. to RECIST 1.1 were comparable. Early & sustained increases of circulating CXCL-10 & IFN-gamma levels were observed.

Table 1.

Efficacy (iRECIST)	**ORR, % [95% CI]**	**Median PFS, mo [95% CI]**
ITT (N=114), investigator read	39.5 [30.5-49.1]	6.9 [4.9-9.3]
By PD-L1 (centrally tested; 22C3)		
<1% (N=32)	31.1 [16.1-50.0]	4.2 [3.6-6.1]
1-49% (N=38)	44.7 [28.6-61.7]	8.3 [4.4-15.7]
≥50% (N=20)	55.0 [31.5-76.9]	11.4 [4.0-16.8]
≥1% (N=58)	48.3 [35.0-61.8]	9.3 [6.3-15.7]

Conclusions: E + P is safe & shows encouraging antitumor activity in 1st line metastatic NSCLC patients unselected for PD-L1, warranting late-stage clinical investigation.

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